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ORIGINAL SUBMISSION

Original submission

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Desanguination Products, LLC

2613 Newcomb
Lubbock, Texas 79415

May 26, 1999

Office of Premarket Approval (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, SW
Washington, DC 20204

Dear Sir/Madam,

Enclosed we are submitting in triplicate a GRAS Exemption Claim, pertaining to the use of a protein preparation, isolated from animal blood, in human foods. The notice is prepared according to the proposed rules published in the Federal Register of April 17, 1997.

Please do not hesitate to contact us if any additional information or documentation is needed.

Sincerely yours,

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GRAS EXEMPTION CLAIM

A. NOTIFIERS.

Johannes Everse, Ph.D. and
Gwynne H. Little, Ph.D., owners
Desanguination Products, LLC,
2613 Newcomb Street
Lubbock, TX 79415

Dr. Everse is also a Professor of Biochemistry at the Texas Tech University Health Sciences Center, and Dr. Little is an Associate Professor of Biochemistry at the same institution. Both applicants are thoroughly familiar with proteins, their properties, separation techniques, oxidation products, etc. as well as with the scientific literature pertaining to this notice.

B. NAME OF NOTIFIED SUBSTANCE.

The substance to which this notice pertains consists of whole animal blood, from which the colored component (the heme), as well as all non-protein components, have been removed, using an oxidative process. It thus consists of naturally occurring blood constituents (proteins), although some of the amino acid residues in some of the proteins may have become oxidized during the process. A product consisting of decolorized animal blood proteins is presently not known or marketed under a common name.

(a) Quantitative Compositions.

The product is a mixture of all the proteins contained in blood. A complete catalog of these proteins is impractical (probably even impossible with current technology). Globin derived from hemoglobin is the major component accounting for about 70% of the total. Albumin accounts for about 10% of the total, with the remainder being made up of small amounts of hundreds of other proteins.

It should be noted that some of these proteins contain amino acid residues that are oxidized as a result of the decolorization process. Thus, some of the cysteine residues have been oxidized to cysteic acid residues and some of the methionine residues are oxidized to methionine sulfoxide. These oxidation products are considered GRAS, because cysteic acid, being a precursor of taurine, is a normal metabolite, and methionine sulfoxide is readily reduced to methionine in the body. The higher oxidation product, methionine sulfone, is not formed during the oxidation process and is not present in the final product.

(b) Common or Usual Name.

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A product consisting of decolorized animal blood proteins is presently not known under a common name. We plan to market our product under the name of "DeSanguin", which is an abbreviation for "Desanguinated Blood Proteins". The term "desanguinated" is a term coined by us to refer to our decolorization process. To our knowledge, it has not been previously used.

C. CONDITIONS OF USE.

Blood from domestic meat animals contains biologically valuable protein equivalent to 6 to 7% of the lean meat content in the carcass (Wismer-Pedersen, 1988). Hence, converting the blood proteins into a product suitable for human consumption will increase the amount of nutrition derived from an animal by 6-7%, which is a considerable increase in the yield of consumable product per head of cattle.

To the best of our knowledge, a protein preparation obtained from animal blood that is similar or identical to DeSanguin is presently not being used in human food products in the US. However, blood proteins, when obtained as a colorless, odorless, and virtually tasteless product, can be used in many different ways as a food product or food additive. Some of the main uses could be:

1. as an additive to baby foods because of its superior nutritional value;
2. as a supplement or additive to dry packaged foods (e.g. soups) to increase their nutritional value;
3. as an additive to canned liquid food products (e.g. soups) to supplement their nutritional value;
4. as a substitute for meat or as an additive to meat in hamburgers, hot dogs, sausages, etc.;
5. as a substitute for soy proteins in many products, since animal proteins have a higher nutritional value than plant proteins;
6. as a food product in the form of solid protein, which can be added to salads, etc. after the addition of suitable coloring and flavorings, as is normally done with Jello;
7. as an emulsifier to prepare fat/protein emulsions, as is presently done using caseinates and soy proteins.

The levels of use in the above-listed products may vary, but we anticipate them to be about the same as those presently used for soy proteins and other plant proteins.

D. BASIS FOR THE GRAS DETERMINATION.

Our basis for the GRAS determination claim is the following:

a. the fact that animal blood as such has been consumed by humans in appreciable quantities since pre-historic times. On that basis we assume that animal blood as such is GRAS.

b. the fact that for many years humans have exposed animal blood to oxidative processes prior to its consumption, including boiling, frying, grilling, etc.

c. the fact that all meats consumed by the US population contains some amount of blood, since it is impossible to remove 100% of the blood from meats. Therefore, blood proteins have been consumed by the US population as long as they have been eating meat. As such, this blood has been exposed to the techniques of food preparation mentioned in the previous paragraph.

d. the fact that, to the best of our knowledge, our product does not contain any component that is not present in prepared meats, including hamburgers and hot dogs, or that is not present in blood-containing foods, such as black puddings, etc., and has therefore not been part of the human diet for hundreds of years.

e. following a thorough search of the relevant literature, the only adverse statements that we have found pertaining to the consumption of blood or blood-derived products are the presence of a disagreeable color, strong odor, and for most people an unpleasant taste. These attributes are no longer present in our final product. Representative items from the literature are enclosed with this notification.

In addition, we use the following logical assumptions:

First, we assume that the separation of a GRAS substance into its components does not alter its GRAS status, unless undesirable chemical reactions have taken place during the separation process.

Second, if chemical reactions do take place during the separation process, but these reactions are equivalent to chemical reactions taking place during the normal preparation of human food (such as cooking a hamburger on a grill), then such reactions do not alter the GRAS status of the product.

Based on these facts and assumptions, we claim that our product DeSanguin is substantially equivalent to one or more GRAS substances that have been part of the human diet for centuries. These GRAS substances are whole animal blood as well as prepared (heated) blood and meats.

(a) Background

Hundreds of millions of animals are slaughtered each year all over the world, and most of these are slaughtered for meat production. Almost all parts of the animals are used for one purpose or another, but thus far the full potential value of the large amounts of blood produced during the slaughtering has not been realized. Some of this blood is used to produce plasma proteins, some is used as an animal feed supplement, and some is used as fertilizer, after it has been converted to blood meal. Much blood, however, is not used in a productive manner and ends up being discarded with attendant environmental consequences.

The number of cattle slaughtered in the U.S. alone is about 30 million annually. Since the weight of an average cow is 1100-1200 lbs (500 kg) and its recoverable blood is about 5% of its body weight, i.e. 25 kg, the total amount of recoverable cow blood produced in the U.S. is 750 million kg or 713 million liters annually. The total amount of protein in blood is 180 grams per liter when the red cell content is included, whereas blood plasma contains only 69 grams per liter. Thus, the cow blood produced annually in the U.S. contains 128.4 million kg or 283.5 million lbs of highly nutritious animal protein, and most of this is wasted. Note

that this calculation does not include blood obtained from the slaughter of 10 million sheep, 79 million pigs, and more than 6 billion poultry annually.

As a source of protein, blood is comparable to lean meat. Blood consists of 80% water, 18% protein, and 0.1% fat, whereas lean meat consists of 75% water, 18% protein, and 3% fat. The amino acid content of blood and meat is also very similar (see Table 1). Unfortunately, up to this time in the U.S. more than 300 million lbs of this rich protein source have been wasted annually, due to the fact that no economical way could be found to convert raw blood into an appealing edible product. As a result, besides wasting a source of valuable protein, the disposal of blood at slaughterhouses has in many instances caused a serious environmental problem, and this problem is going to be considerably more serious in the next century, when the number of animals slaughtered will increase considerably. Therefore, a procedure that economically can convert blood into a useful product is urgently needed, and will be of benefit to humanity in more ways than one.

(b) History of Using Blood in Human Foods.

Wismer-Pedersen (1988) states that about 10% of the blood produced in Swedish abattoirs is used for blood-containing foods. For Ireland and Germany this number is about 5%, whereas about 2% is used in Denmark. In Russia, decolorized blood proteins are mixed with an equal amount of egg powder, and then used in sausages, etc. The Kiev Meat Packing Plant in Kiev produces 80-100 tons of this mix per year (Gorbatov, 1988). In the US the use of animal blood in human foods is quite limited; however, recipes for the use of animal blood in blood sausages, black puddings, and as a thickener for sauces can be found in many popular cookbooks (e.g., Rombauer and Becker, 1981).

It should be evident from this that, except for its undesirable color and strong taste, no adverse properties have been associated with the use of animal blood or blood products in human diets over many years.

As mentioned, the main problem with using blood as a source of edible protein is its undesirable dark color as well as its unpleasant odor and strong taste. These characteristics are due to the presence of hemoglobin, the major protein of blood. Hemoglobin consists of a protein part (globin) and an iron-containing porphyrin ring (heme); this heme gives blood its red or brown color as well as its strong taste. These objectionable properties of blood could be eliminated by the development of a suitable method to eliminate the heme component of hemoglobin. Because the potential nutritional and commercial value of animal blood proteins has been recognized for a long time, a number of procedures have been developed and patented in the past to remove the heme from whole blood or from red cell hydrolysates. However, although the heme is not covalently bound to the globin protein, its removal has proven to be quite difficult, due to its insolubility in water and its high affinity for hydrophobic proteins and membranes. Past approaches to this problem are listed in the accompanying literature as well as in a number of relevant patents (see Literature list).

Some attempts to remove the heme from whole blood involved an extraction of the

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heme using organic solvents. Unfortunately, the heme molecule is not easily removed in this manner; it does not dissolve very well in most organic solvents. It is moderately soluble in aromatic solvents, such as benzene and toluene, but it is quite difficult to remove the last traces of these solvents from the remaining protein solution. The latter is essential, because these solvents themselves are quite toxic and are also suspected carcinogens. Some success was obtained by using acid acetone to extract the heme (Tybor et al., 1975); however, the cost of acetone and its high evaporation rate made this approach not economically feasible.

Other approaches were published by Sato et al. (1981) and Autio (1983), who used absorption of the heme on carboxymethyl cellulose to remove the heme portion of the hemoglobin. Similarly, Mellkvist (1979) developed a filtration process, Hald-Christensen et al. (1981) claimed an enzymatic process for blood decolorization, whereas Piot et al. (1987) used absorbents, such as alumina and magnesia, to achieve the same. These, however, are quite expensive processes that limited their commercial use.

A different approach has been to oxidize the heme with hydrogen peroxide (Bingold, 1949; Mitsyk and Osadchaya, 1970; Oord and Wesdorp, 1979). Although heme is effectively oxidized by hydrogen peroxide, the use of hydrogen peroxide in whole blood has been hampered by the fact that hydrogen peroxide is rapidly inactivated by catalase, an enzyme that is abundantly present in blood. Inactivation of the catalase has been done by heating the blood to a temperature above 60°C (Buckley et al., 1979) and by acidification of the blood prior to treatment with hydrogen peroxide (Piot et al., 1987).

More recently, Wismer-Pederson (1988; 1992) disclosed a procedure for the production of a heme-free protein product from blood in which most of the heme is precipitated by acidification of the blood and subsequently removed by centrifugation. The remaining heme is then oxidized by hydrogen peroxide or any one of a number of inorganic peroxides. This procedure has the advantage over previous procedures that it requires much less peroxide to oxidize the heme, but its disadvantages are that it is lengthy and requires the use of expensive equipment for the removal of the precipitated heme.

Most recently, D.R. De Buyser (1999) described a procedure in which whole blood or a blood hydrolysate is brought to a pH above 12, using an alkaline solution, and then treated with hydrogen peroxide at pH 10.5 to oxidize the heme. The remaining protein is then precipitated and separated from the oxidation products by centrifugation.

These examples illustrate the considerable efforts that have continuously been expended in attempts to recover this valuable protein source for human use. Unfortunately, efficient decolorization by methods so far evaluated by industry has turned out to be too costly in comparison to the price of meat, milk, and vegetable proteins (Wismer-Pedersen, 1988). Nevertheless, it seems reasonable to assume that people would not have put in the efforts and expenses unless they fully expected to gain a product that would be suitable for human consumption. This confidence is also expressed by Wismer-Pedersen (1988), who states that it is reassuring that in a world with a great many people suffering from

malnutrition and even hunger, a readily available protein reserve is waiting for utilization.

(c) Decolorization Process.

The exact process used by us to convert whole animal blood into DeSanguin is the subject of a present patent application; appropriate confidentiality is therefore requested. Briefly, an anticoagulant (sodium citrate) is added to the blood immediately upon collection from the carcasses. Subsequently, the heme portion of the blood is oxidized using an approved oxidizing agent. The blood proteins are then separated from the non-protein components of the blood as well as from excess reagents and oxidation products by a traditional dialysis-type procedure. Finally, water is removed by a suitable drying process. All the chemicals used during the procedure are in the EAFUS database and are used only during processing. They are not present in the final product.

Thus, we have developed a process by which protein can be recovered from blood using relatively small amounts of inexpensive chemicals that have been approved for use in the preparation of human foods. The product obtained is odorless, tasteless, virtually colorless, and water soluble.

(d) Safety of Starting Material.

It is presumed that the blood used in the preparation of DeSanguin will be obtained at slaughterhouses in a manner that prevents contamination, and that the sanitary collection of blood will be monitored by the inspectors and agencies that currently are responsible for assuring the safety of meat and meat products. As stated above, our process for the recovery of the protein from the blood uses only substances from the EAFUS database and these are used during processing only. They are eliminated from the final product, which consists almost entirely (>99%) of animal protein.

Affirmation of blood proteins as GRAS must, of course, be based on the presumption that the protein is derived from blood that is appropriately obtained. Two requirements will apply to the collection of animal blood that will be processed for human use. First, that only blood from animals that have passed inspection will be collected for this purpose, and second, that the collection of the blood will be done such that it remains uncontaminated. Both requirements will have to be implemented in the abattoirs.

The inspection of carcasses in the slaughterhouses is routinely done at the present time. Hence, the blood from each carcass needs to be kept separate from that of other carcasses until the inspection has taken place and the carcass is approved. After approval of the carcass the blood can be pooled and processed. This will satisfy the first requirement.

To satisfy the second requirement, the collection of the blood will have to be done in a manner that prevents its contamination that could occur if the blood comes in contact with the outside of the carcass. This is done by collecting the blood using hollow knives that are attached with a hose to plastic containers. The knives are sterilized after each use. Such a procedure is described in detail by Knipe (1988); such procedures are routinely used in some

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European countries.

(f) Substantial Similarity To A GRAS Substance.

We claim that the simple removal of certain components from a GRAS substance does not alter its GRAS status. For example, the removal of water from milk (converting milk to milk powder) or the separation of the egg white from whole eggs does not alter the GRAS status of the separated product. Therefore, the removal of certain non-protein components from animal blood should also not change the GRAS status of blood into a non-GRAS product.

We recognize, however, that in addition to the separation of the proteins from the non-protein components of blood, our process involves an oxidation of the heme portion of the blood. As a side reaction, this oxidation process results in the simultaneous oxidation of part of the cysteine and methionine residues of the blood proteins, rendering them non-equivalent to the proteins present in the original blood. We claim nevertheless that our product is still equivalent to a GRAS product, for two reasons. First, the various oxidation products of cysteine and methionine, which include cystine, cysteic acid, methionine sulfoxide and methionine sulfone, are present in various heated (cooked) foods, and are abundantly present in foods such as well-done grilled steaks, hamburgers and hot dogs, where the oxidation occurring during the heating often extends to the point of converting some of the proteins to charcoal. Secondly, to the best of our knowledge, and in agreement with the first statement, none of these products have scientifically been shown to be harmful to humans at any time.

Further evidence is provided in Table 1, which shows the essential amino acid contents of our product (DeSanguin) in comparison to that of whole blood, blood protein preparations from others, soy proteins and casein. It is clear that there is a great similarity in the amino acid constitution of these various products. In addition, we have included the amino acid analysis profiles of whole cow blood (Sample HCl #1) and that of our final product (Sample HCl #2). These profiles show clearly that our product does not contain any "peaks" that are not present in the original blood sample, indicating that no new and unknown amino acid residues were formed during the manufacturing process.

(g) Conclusion.

In conclusion, we have presented considerable evidence indicating that our blood protein product should be safe to use in human foods. This indication is further supported by the enclosed literature, which are representative of the available literature pertaining to the subject of this notification. As scientists with expertise in the subject area we firmly state that at this time we are unaware of the existence of any published information that is not in agreement with this conclusion.

E. AVAILABILITY OF INFORMATION.

We hereby affirm that the data and information that form the basis for our claim for GRAS status of our product are available for review and copying by FDA or will be sent to FDA upon request. The following relevant publications are enclosed with this notification:

Wismer-Pedersen, J. (1988). Use of Haemoglobin in Foods - A Review. Meat Science **24:** 31-45.

Dill, C.W. and Landmann, W.A. (1988). "Food Grade Proteins From Edible Blood". In: **Edible Meat By-Products.** A.M. Pearson and T.R. Dutton, Eds., Elsevier Applied Science, New York. Chapter 5.

Knipe, C.L. (1988). "Production and Use of Animal Blood and Blood Proteins for Human Food". In: **Edible Meat By-Products.** A.M. Pearson and T.R. Dutton, Eds., Elsevier Applied Science, New York. Chapter 6.

Gorbatov, V.M. (1988). "Collection and Utilization of Blood and Blood Proteins for Edible Purposes in the USSR". In: **Edible Meat By-Products.** A.M. Pearson and T.R. Dutton, Eds., Elsevier Applied Science, New York. Chapter 7.

Rombauer, I.S. and Becker, M.R. (1981). The Joy of Cooking. The Bobbs-Merrill Company, Inc., Indianapolis, 338-339, 496-497, 810.

Press release of the Associated Press, entitled "Brazil uses cow blood to fight malnutrition", published in the Lubbock Avalanche Journal of March 18, 1996.

F. LITERATURE CITED:

Autio, K., Kiesvaara, M. and Malkki, Y. (1983). Method for Dividing Blood Hemoglobin Into Heme and Globin. US Patent # 4,518,525.

Bingold, K. (1949). Entstehung des Pentdyspents und seine Bedeutung Fur den Haemoglobin-stoffwechsel. Deutsches Archiv fur klinische Medizin **195:** 413.

Buckley, K., Vernon, A. and Lowe, P.J. (1979). Food Protein Product. US Patent # 4,180,592.

De Buyser, D.R. (1999) Protein Product from Blood and/or Hemoglobin. US Patent # 5,880,266.

Gorbatov, V.M. (1988). "Collection and Utilization of Blood and Blood Proteins for Edible Purposes in the USSR". In: **Edible Meat By-Products.** A.M. Pearson and T.R. Dutton, Eds., Elsevier Applied Science, New York. Chapter 7.

Hald-Christensen, V., Adler-Nissen, J.L. and Olsen, H.S. (1981). Method for Preparing a Food Material From Blood. US Patent # 4,262,022.

Knipe, C.L. (1988). "Production and Use of Animal Blood and Blood Proteins for Human Food". In: **Edible Meat By-Products.** A.M. Pearson and T.R. Dutton, Eds., Elsevier Applied Science, New York. Chapter 6.

Mellkvist, C-O. (1979). Filtration Process. US Patent # 4,152,260.

Mitzyk, V.E. and Osadchaya, I.F. (1970). Quality of Clarified Animal Blood and of Food Products with Additions of this Blood. Tovarovedenie **8**: 67.

Oord, A.H.A. and Wesdorp, J.J. (1979). Decolouration of Slaughterhouse Blood by Treatment With Hydrogen Peroxide. 25th Europ. Meeting Meat Res. Workers, Budapest. Paper 10.7 (quoted in Wismer-Pedersen, 1988).

Piot, J-M., Guillochon, D., Charet, P. and Thomas, D. (1987). Process for Decoloring Substances Colored By Tetrapyrrole Compounds. US Patent # 4,650,589.

Rombauer, I.S. and Becker, M.R. (1981). The Joy of Cooking. The Bobbs-Merrill Company, Inc., Indianapolis, 338-339, 496-497, 810.

Sato, Y., Hayakawa, S. and Hayakawa, M. (1981). Preparation of Blood Globin Through Carboxymethyl Cellulose Chromatography. Food Tech. **16**: 81.

Tybor, P.Y., Dill, C.W. and Landmann, W.A. (1975). Functional Properties of Proteins Isolated From Bovine Blood by a Continuous Process. J. Food Sci. **40**: 155.

Wismer-Pedersen, J. (1988). Use of Haemoglobin in Foods - A Review. Meat Science **24**: 31-45.

Wismer-Pedersen, J. (1992). Process for Producing a Substantially Heme-Free Blood Protein. US Patent # 5,151,500.

Table 1

Essential Amino Acid Composition of Blood and Various Blood Products In Comparison to Other Commercial Protein Products (gr/100gr)

	1	2	3	4	5	6	7	8	9
Essential Amino Acids	DeSanguin	Blood cow (DeB)	Blood cow (ours)	Well-done hamburger	Raw meat used for hamburger	Globin (DeB)	Globin (W-P)	Na-caseinate	Soy isolate
Isoleucine		1.2	1.02	4.9	3.9	0.6	0.44	5.7	5.0
Leucine		12.9	12.16	8.4	7.0	14.5	13.78	10.0	8.5
Lysine		9.3	8.80	8.1	7.7	7.5	9.0	8.5	7.0
Methionine		0.9	1.74	2.6	2.3	0.8	0.76	2.9	1.4
Cyst(e)ine		1.3	1.27	1.4	1.2	0.9	0.64	0.4	1.4
Phenylalanine		6.9	5.63	3.2	2.7	7.3	6.8	5.5	5.4
Tyrosine		3.0	1.96	2.8	2.0	1.4	1.48	6.1	3.4
Threonine		4.3	5.15	4.5	4.0	3.7	3.0	4.9	4.2
Tryptophan		N.D.	0.98	N.D.	N.D.	N.D.	0.9	N.D.	N.D.
Valine		9.5	9.91	6.0	5.3	10.4	10.24	7.1	5.2

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NOTES TO TABLE 1.

1. Values for cow blood and globin marked "DeB" (columns 1 and 6), as well as the values for Na-caseinate and soy isolate are taken from a table published by De Buyser, 1999, US Patent # 5,880,266.

2. Values for globin marked "W-P" (column 7) are taken from a table published by Wismer-Pedersen, Meat Science **24**: 31-45, 1988.

3. A well-done hamburger was purchased from a local "Denny's" restaurant, together with some of the raw meat of the frozen patty used to make the hamburger. The fat was extracted from the meat prior to hydrolysis of the protein. The amino acid analyses of these products are shown in columns 4 and 5.

4. Hydrolysis and amino acid analyses of samples from our laboratory (columns 1, 3, 4, and 5) were performed by The Laboratory For Protein Chemistries, Texas A&M University, College Station, TX 77842.

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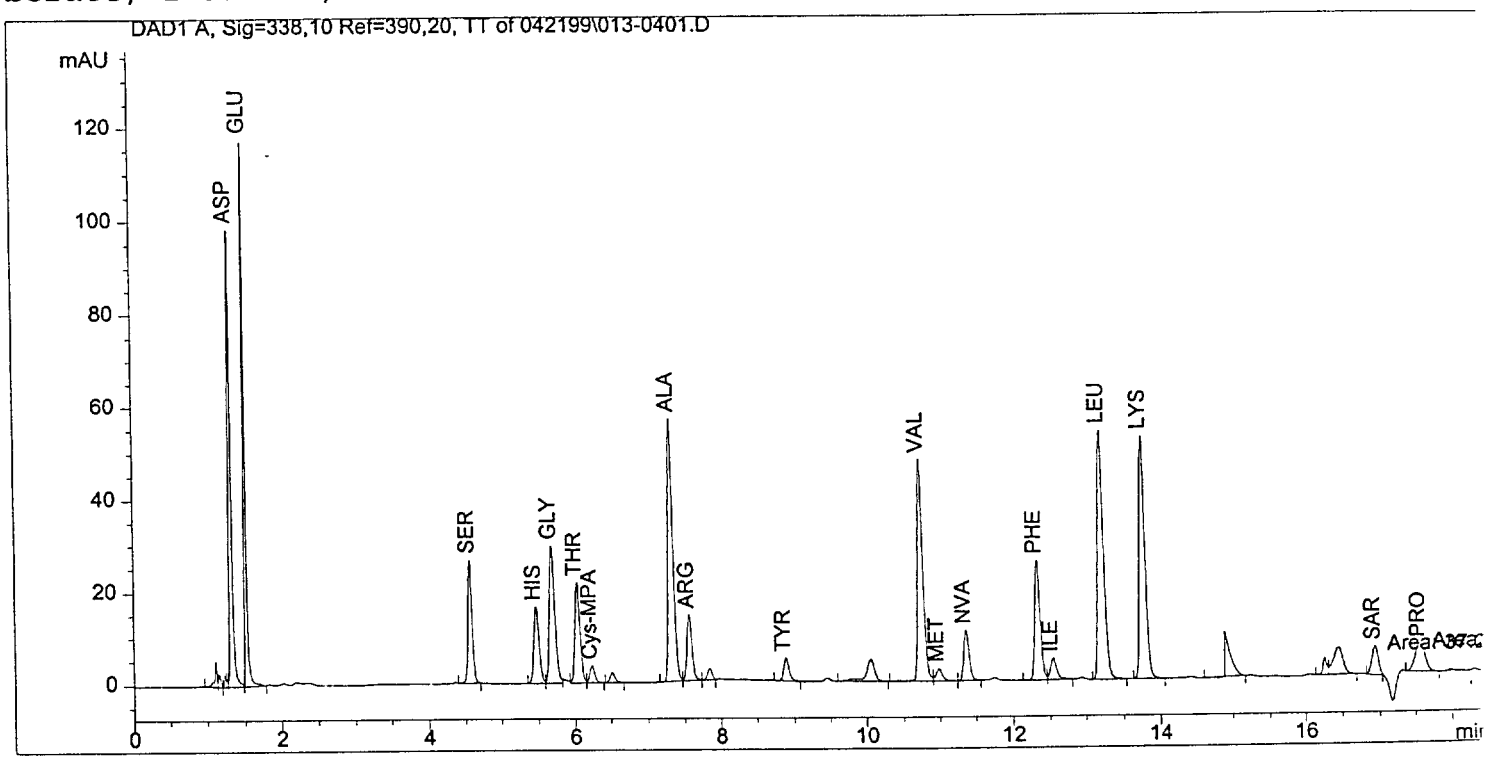
Injection Date : 4/21/99 4:51:28 PM
Sample Name : HCl #1
Acq. Operator : (b) (6)

Seq. Line : 4
Vial : 13
Inj : 1
Inj Volume : Inj prog

Acq. Method : C:\HPCHEM\1\METHODS\DAD-1.M
Last changed : 4/15/99 1:19:24 PM by (b) (6)
Analysis Method : C:\HPCHEM\1\METHODS\042199.M
Last changed : 4/22/99 11:21:23 AM by (b) (6)
(modified after loading)

DAD-1: Detected by FLD and UV detector. One microliter injection, 4 ul borate, 1 ul OPA, 1 ul FMOC



Internal Standard Report

Sorted by Signal
Calib. Data Modified : Thursday, April 22, 1999 10:53:03 AM
Multiplier : 1.000000
Dilution : 1.000000
Uncalibrated Peaks : not reported

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Injection Date	: 4/21/99 6:04:02 PM	Seq. Line	: 6
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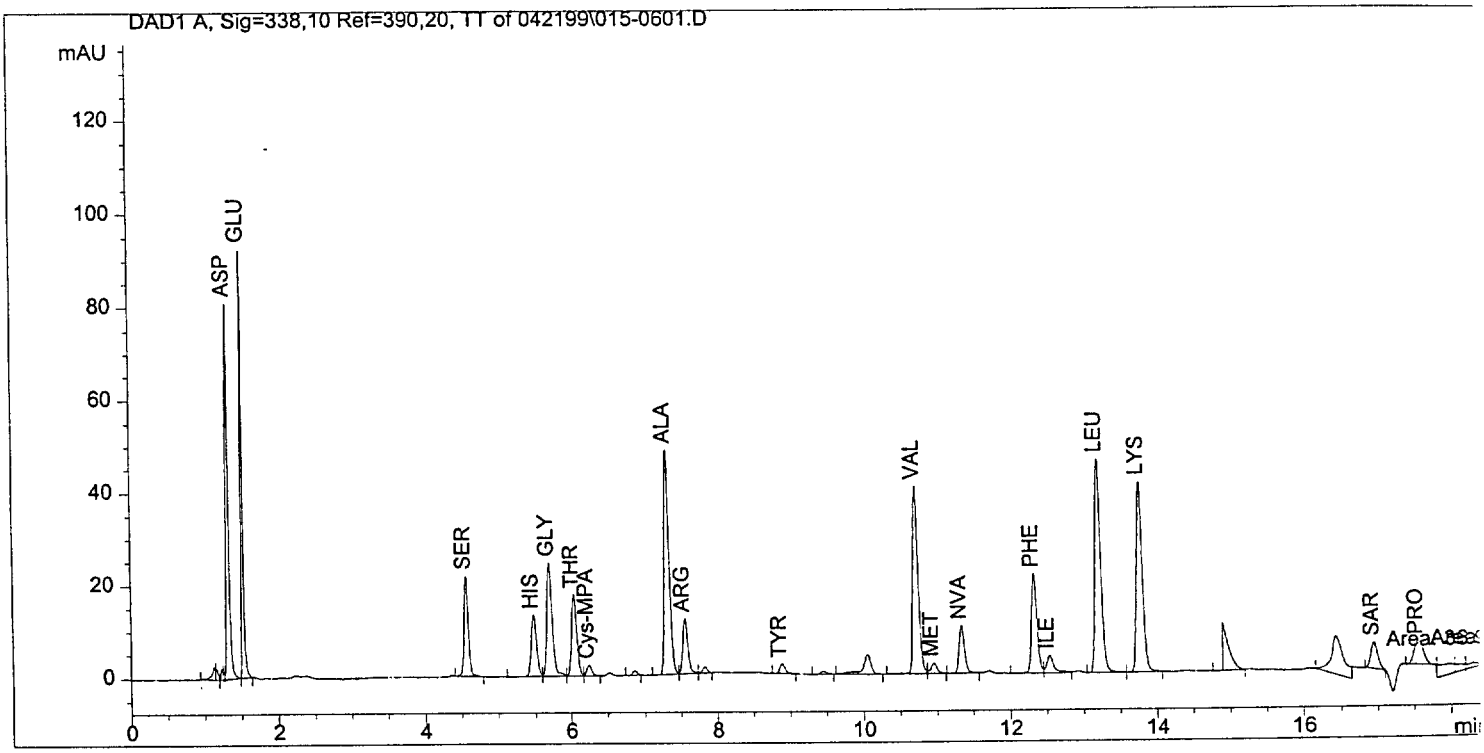
Acq. Operator	: Jinny Johnson	Inj	: 1
		Inj Volume	: Inj prog

Acq. Method : C:\HPCHEM\1\METHODS\DAD-1.M
Last changed : 4/15/99 1:19:24 PM by Jinny Johnson
Analysis Method : C:\HPCHEM\1\METHODS\042199.M
Last changed : 4/22/99 10:54:53 AM by Jinny Johnson
(modified after loading)

DAD-1: Detected by FLD and UV detector. One microliter injection, 4 ul borate, 1 ul OPA, 1 ul FMOC



Internal Standard Report

Sorted by Signal
Calib. Data Modified : Thursday, April 22, 1999 10:53:03 AM
Multiplier : 1.000000
Dilution : 1.000000
Uncalibrated Peaks : not reported

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SUBMISSION END

Submission End

000077

To: Maribeth LaVecchia@OPA@FDA.CFSAN
From:
Certify: N
Priority: Normal
Subject: RE: Follow-up to our telephone conversation
Date: Thu Jun 24 09:22:37 1999
Attached: None

AM

Dear Dr. LaVecchia:

Thank you for your assistance in locating additional FDA information. We also appreciate your taking the time to talk with us on the telephone this morning. You and your colleagues were most helpful.
We are grateful for the rapid and substantive response to our GRAS notification. It is very helpful that the process has proceeded this point so quickly. While we were prepared for the possibility that you would require additional information we had feared that a year might pass before we learned what else we needed to do.

Per our telephone conversation, we will either clarify our GRAS petition, within 30 days, along the lines we discussed or we will submit a food additive petition.

Thank you again for your help.

Johannes Everse
Gwynne H. Little

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Happy Mail!

To: Maribeth LaVecchia@OPA@FDA.CFSAN
From:
Certify: N
Priority: Normal
Subject: GRAS notification
Date: Thu Jul 08 13:49:44 1999
Attached: None

AM

Dear Dr. LaVecchia,
Referring to our phone conversation of June 23, and your e-mail of the same date, I am taking you up on your invitation to contact you whenever we had any questions concerning the decision that you asked us to make regarding our GRAS notification. We have several. They arose mostly after reading all the material that you suggested in your e-mail.
First of all, during our telephone conversation you asked us about our method of preparing the protein from animal blood. The reason we were somewhat hesitant is really a matter of patent protection. Although blood proteins have been known for eons, the manner of preparing them can be unique, and in our case, we are indeed in that position. That put us in a dillemma:
Our product is really not worth anything unless it can be used for human consumption, which requires FDA approval for such. It seems unwise to spend lots of money seeking a patent, unless we can be reasonably assured that approval can be obtained. But applying to the FDA includes publication of all procedures, etc., which in turn jeopardizes any future patent applications. How do we deal with this? I'm sure you have dealt with this before.
Second, if we apply for our product to be used as a food additive, two requirements apply that we don't know how to deal with. 1. The rules state that one has to test the additive at 100 times the level that may be used in foods. Thus, if the protein is used as a meat supplement in hot dogs or hamburgers, for example, where easily 20 to 30 grams may be added to a hamburger, one would have to test the product at levels of 2 to 3 kg. It would take a herd of elephants to do that. 2. The rules state that one has to provide methodology that allows one to determine the exact amount of additive that is present in food. Since adding our product, which consists of denatured proteins, to hamburgers or hot dogs or other foods that also contain denatured proteins, we know of no way by which one can distinguish one from the other, either immunologically, biochemically, or otherwise. How do we deal with that?
Third, are we perhaps putting the cart before the horse in seeking FDA approval? From the regulations and from the information that you provided we are getting the feeling that perhaps it should be the companies that intend to add our product to their foods that should be applying instead of us. The reason being, that you require detailed information about the composition of the foods to which the additive is to be added, information that would normally not be available to us, only to the potential user. Do we see this wrong?
We would very greatly appreciate your comments, because we are somewhat stuck in making a choice between continuing our application for GRAS status, or changing it to a food additive petition.
Thank you so much for your time and guidance.
Jo Everse

Happy Mail!

AM

Desanguination Products, LLC

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July 29, 1999

Dr. Maribeth LaVecchia
Division of Petition Control (HFS-215)
Office of Premarket Approval
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, SW
Washington, DC 20204

1999 AUG -2 P 2:49

Dear Dr. LaVecchia,

This letter is in response to our phone conversation and your e-mail responses to our queries. After carefully considering your information and advice, we have decided that it would be better for us to wait seeking FDA approval for our product until after we have applied for patent protection for same. You stated that in your experience, this is the way most petitioners deal with privileged procedures, etc.

Therefore, we hereby request the Commissioner to withdraw our GRAS Notification, dated May 26, 1999, without prejudice to a future filing.

We thank you and your colleagues for all the information and advice that you have given us. All this will be very helpful to us when we contact the FDA again concerning our product.

With best regards,

Sincerely yours,

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NA- Not applicable